Section of Measurement in Medicine

President Sir George Godber KCB DM

Meeting October 26 1964

Inaugural Meeting

The Inaugural Meeting of the Section of Measurement in Medicine of the Royal Society of Medicine was held at 1 Wimpole Street, London W1, on Monday, October 26, 1964, at 8.0 p.m., with the Rt Hon Lord Cohen of Birkenhead, President of the Society, in the Chair.

Objects of the Section
(*a*) To provide a forum where physicians and surgeons may discuss and assess technological developments which might be used to advance knowledge of the diagnosis and treatment of disease.

(*b*) To make available information of an electronic, engineering and biophysical nature and to consider the opportunities for its application in clinical medicine.

(*c*) To discuss the applications of technological development to various fields of medical research.

(*d*) To assist in the training of those with clinical responsibilities in the techniques of instrumentation and measurement.

(*e*) To aim at the achievement of these objectives by frequent collaboration with other Sections of the Society.

It was proposed from the floor that the objects of the Section could be succinctly stated as 'the promotion of the understanding and proper use of quantitative techniques in clinical practice and research', and this suggestion received the approval of the Meeting.

Opening Address

by the Rt Hon Lord Cohen of Birkenhead MD
(*President of the Royal Society of Medicine and President of the General Medical Council*)

It is a great pleasure and a high privilege as President of the Royal Society of Medicine to welcome most warmly to the comity of our Sections its most recent and 29th member – the Section of Measurement in Medicine. It is not surprising that this Section should enter so late into the Society's activities, for mensuration appears late in the advance of medical knowledge. It is true that the Arabs had introduced techniques of physical measurement into their science, and in all forms of ancient medicine from Egypt to Greece (and indeed persisting still amongst the ignorant) there was much number-lore associated, for example, with the number three or its multiples for luck, good or bad, and seven and its multiples for supernatural powers. The influence of the Chaldean number-lore of Pythagoras is exemplified in the Hippocratic doctrine of crises and critical days, which assigned fixed periods to the resolution of different diseases.

But the demise of myth and the birth of measurement in the investigation of nature stems from the University of Padua, which as late as 1670 was described as 'the Imperial University for Physic for all others in the world.' Of all European Universities in the sixteenth century Padua was the least shackled by authoritarianism. In 1404 it had fallen under the rule of Venice which was at that time, and for long after, the most anticlerical state in Europe. In it, quantitative methods of investigation were soon introduced into the physical and biological sciences. The search there was not for the final causes of the theologian who asked 'why?' Indeed, in a University so highly secularized as Padua doubts were to be expected about the part which final causes played in natural philosophy. The question 'how?' assumed greater importance than the question 'why?'

Thus it is not surprising that in the University which nurtured Vesalius, Copernicus, Sanctorius, Galileo and Harvey, to mention only the peaks of a long and high mountain range of achievement, there was accurate observation of natural phenomena, and their explanations were sought on a mechanical and quantitative basis. Indeed, the principle of science as understood by Galileo was that 'nothing is scientifically knowable except what is measurable'.

Since then none familiar with the evolution of medicine will doubt that many of its most explosive advances, especially in the last few decades, have resulted from the application of the quantitative method in medicine and the devising of increasingly accurate instruments and techniques for experiment and for the analysis of the data which result. Many of these instruments reflect the joint efforts of doctors and those working in other scientific disciplines – engineering (mechanical, electrical, electronic, radio), physics, chemistry, mathematics (in recent years especially the computer programmer and analyst) and indeed the philosophers and historians of science, whose contribution to our knowledge of the nature of concepts and the fundamental laws of science is sometimes overlooked. Perhaps too little tribute has been paid to the late Norbert Wiener, whose cybernetic theory demonstrated the full potential of the contribution which the synergy of these disciplines could make to the advance of knowledge.

I earlier emphasized that from the days of Hippocrates until the end of the sixteenth century medicine was essentially descriptive. The sick were observed and the courses of their diseases were recorded. For example, not only was fever recognized by the ancients, but 'specific heats' were later held to be pathognomonic of certain diseases, and as recently as fifty years ago some physicians were still speaking of the 'pungent' heat of scarlet fever as a diagnostic feature of this disease. Various types of pulse – strong, weak, full, slow, rapid, &c. – had also been noted by many of the older writers. The differing 'temperaments' of individuals had been recognized and explained on the basis of Plato's humoral theory which persisted, and indeed dominated medical theory and practice, until the early nineteenth century.

The earliest attempts to apply measurement to medicine were not unexpectedly cradled at Padua. Mettler states that whilst Galileo was a student there he used the pendulum to measure the rate and variation of the pulse, but the earliest record of its use is to be found in a small book on differential diagnosis published in 1602 by Santorio Santorio, or Sanctorius, the name by which he preferred to be known. Sanctorius was a graduate of Padua and in 1611 was appointed to its Chair of Medicine. He described how by using a ball attached to a piece of string as a pendulum the length could be adjusted until the beat of the pendulum coincided with that of the pulse (*pulsilogium* or pulse-clock); thus the rates of pulses could be compared by the varying length of the pendulum. In 1612, in his commentary on Galen's medicine, Sanctorius described how temperature could be measured, and in 1625 in his commentary on Avicenna he gave details of the use of his thermometer, both manually and orally, in the study of disease. In this work are to be found descriptions and illustrations of various types of thermometers then in use. Galileo also devised a thermometer but Sanctorius appears to have priority.

Sanctorius was also a pioneer in quantitative metabolic study, and for this purpose invented a counter-balanced steelyard chair. It had long been known that a person eats more food than is necessary for growth, and more than can be accounted for by the amount of fæces and urine passed. The gap was said to be due to loss of substance by 'insensible perspiration'. Sanctorius used this steelyard chair to calculate his gradual postprandial loss of weight, and believed that it could be used also in the regulation of diet, since if meals be eaten in the chair its descent would indicate that the diner had consumed a sufficient quantity of food.

Studies in thermometry were developed by George Martine (1740), James Currie of Liverpool in the eighteenth century, and Wunderlich (1868); and in 1870, Clifford Allbutt introduced the short clinical thermometer which made available to all doctors a ready method of ascertaining a patient's temperature. Later methods of continuous recording of body temperature (also of pulse, blood pressure, &c.) owe much to the fruitful co-operation of the medical investigator with other scientists.

William Harvey, himself a product of Padua, brought quantitative considerations to support his experimental demonstration of the circulation of the blood by showing that if the Galenical theory were valid 'it is manifest that more blood passes through the heart in consequence of its action than can either be supplied by the whole of the ingesta, or than can be contained in the veins at the same moment'.

I referred earlier to the pulse rate. It is interesting to note that until the beginning of the eighteenth century, no watch measured minutes. Watches were calibrated in hours and, therefore, were clearly unsuited to measuring the pulse rate. In 1707 Sir John Floyer, a distinguished physician of Lichfield, invented a minute watch and with this he made interesting observations on pulse rates. It was not, however, until a century and a half later that it became common for physicians to take the pulse – an indication of the delay which occurs between the acquisition of knowedge and its clinical application.

Graphic methods of recording the form of the pulse were initiated by Vierordt's sphygmograph in 1855; this was to lead by various modifications to Mackenzie's polygraph (1902) and his brilliant work on cardiac arrhythmias.

The recording of blood pressure dates from the classical experiments of the Reverend Stephen Hales, vicar of Teddington, which were published in 1733. He inserted a brass tube into the femoral artery of a mare and attached to it, after ligaturing the artery, a vertical glass tube so that when he untied the ligature the blood rose in the glass tube to a height of about 2·5 metres. In 1828, Poiseuille one of the pioneers in hæmodynamics, introduced the mercury manometer and others, including Marey and von Basch, later developed the smaller mercurial sphygmomanometer for clinical use. The von Basch sphygmomanometer devised in 1880 was greeted by the *British Medical Journal* with the comment that 'by such methods we pauperize our senses and weaken clinical acuity', which evokes the reflection that although history may not repeat itself, historical situations recur.

In the second half of the nineteenth century we see quantitative methods, using simple instruments, being introduced into a much wider field.

The hæmocytometer was discovered by Vierordt in 1852, and the hæmoglobinometer still commonly in use when I was a student was that of Gowers devised in 1878. About the middle of the past century spirometers were being used to measure what was thought to be the capacity of the lungs and applied to the investigation of chest diseases.

Quantitative methods in applying chemistry to clinical investigation developed much later, doubtless because progress in this field was hindered by the concept of vitalism which dominated biological thought until 1828. It was then that Wöhler converted ammonium cyanate by heating into urea, and for the first time showed that an organic substance could be derived from inorganic material. Prout had shown in 1824 that hydrochloric acid could be found in the stomach secretions, but it was not until 1875 that Carl Ewald was to use the amount of hydrochloric acid as an index of gastric disorder. Urine analyses for albumin and sugar were rapidly developed but methods of quantitative blood analysis were hampered by the amount of blood required for these. However, Claude Bernard, Pavy and Alexander Garrod, the father of Archibald Garrod of 'Inborn Errors of Metabolism' fame, all published work on blood analysis. Alexander Garrod in 1850 estimated the uric acid content of the blood (he was an authority on gout) by hanging a string in a known quantity of blood and allowing the uric acid to crystallize on it. His results compared favourably with those of modern methods.

Shortly after the opening of the twentieth century more accurate quantitative analytical methods for use on very small amounts of blood were devised. The pioneer work of Folin, Wu and Benedict, laid the foundations of much contemporary biochemistry. Without an accurate method for the estimation of blood sugar it is very doubtful if insulin would have been discovered.

It is not surprising in the face of these successes that during the past few decades the investigation of disease in man has been predominantly by the techniques and instruments of physics and chemistry. And with each advance more delicate instruments have resulted and wider fields opened.

The capillary electrometer used by A D Waller in 1889 for recording the electrical changes accompanying the heart beat was replaced in 1902 by the Einthoven string galvanometer which occupied a small room. The modern electrocardiograph can be contained in a large coat-pocket. Electroencephalography, electromyography, and electrical recordings of all types in physiology and medicine, have made noteworthy advances in recent years.

I well recall that in 1918, as a second year medical student, I attended a lecture on isotopes by F W Aston, who had worked in Rutherford's laboratory. No one could then have foreseen the immense contribution which the use of radioactive isotopes has made to our knowledge of metabolism and biochemistry, and to the treatment of disease. Chromatography, electrophoresis, X-ray diffraction – indeed practically every advance in the techniques of physics and chemistry – have found their application in measurement in medicine. When I was first working on carotene metabolism, twenty-five years ago, one estimation of carotene in blood took about six hours, and one was responsible for one's own arithmetical calculations. Today, with a recording ultra-violet spectrophotometer, several and more accurate estimations can be carried out in a very short time. Again, by the use of autoanalysers hundreds of analyses can be undertaken and accurate records produced, in the time taken formerly by a very few analyses, and the energy involved, both physical and mental, is minimal.

The introduction of computers into medicine has assisted us in carrying out with unbelievable rapidity and accuracy intricate mathematical manipulations, and these are destined to play a most important role in assisting in the analysis of medical records, the recognition of similar patterns recurring in a mass of data which could well defy human analysis, in the retrieval of medical information and literature, and in many other ways.

A few months ago, I visited an industrial pharmacological laboratory in the United States and saw in progress there psychopharmacological experiments designed to determine in monkeys the time of recall of an event. A conditioned reflex was induced by which a certain signal produced a reward. The period of time which elapsed before the conditioned reflex was broken was determined and then various drugs were to be tried to increase this time of recall. The whole of this experiment on 100 monkeys was being carried out by electrical recording on tape to be later subjected to computer analysis.

Medical Statistics

Thus far we have considered measurements in the individual, but there are other measurements of medical interest which are applied to groups of persons in health and disease and to populations.

Pierre Charles Alexandre Louis founded medical statistics. Whilst in Poland, whither he had emigrated, he found himself impotent to deal with a diphtheria epidemic. This convinced him of the need for deeper study, and he returned to Paris, entered Chomel's clinic, and having found that the systems and theorizing of the past were sterile, he sought the solution to his problems in facts and figures. He wrote:

> 'After having grouped my cases in respect of their outward analogies, I enquired how many times any given morbid change or symptom existed in each group ... in order to determine their true value: for symptoms or lesions which present themselves invariably in a given disease, are of vast importance, and become more and more insignificant in proportion as they occur less frequently.'

Although Louis's argument is by no means valid he was led by his method to 'counting the symptoms or anatomical changes occurring in cases grouped according to their apparent analogies', and this in spite of what he had been taught and seriously believed, that medicine is a science of observation and of observation only. His work on phthisis in 1825 and on typhoid in 1829 were followed by the statistical proof that blood-letting, so strongly advocated by Broussais in pneumonia, is of little value in this disease. Louis's work and methods are woven into the fabric of the history of medical statistics. Indeed, it led in 1832, to a precursor of this Section – the Société Médicale d'Observation – whose objects were to further the numerical method. Louis was its Life President and it attracted many foreign members, including Marshall Hall.

But the innovator in medicine has never lacked his critics or detractors. Even Claude Bernard doubted the validity of a general application of the numerical method to biological facts though he divined the important truth that 'statistics can yield only probabilities, never certainties'.

Again, Trousseau, the outstanding French clinician of the mid-nineteenth century, also expressed his scepticism about the application of the numerical method. He explained that he took no exception to it, for 'counting is needed in expressing results systematically', but he continued: 'I disapprove of it because it holds fast, like the mathematician, to a rigid result. ... This method is, indeed, the enemy of the doctor; it produces an accountant, a passive servant of figures, which he has affixed to his patient. ... It stifles his intelligence.'

There were, of course, justifiable criticisms of Louis's work. His samples were often inadequate in number and stratification, they often lacked adequate controls, and he himself did not command the appropriate mathematical techniques for the full analysis of his data. Yet Louis's work paved the way to the triumphs of current numerical analyses in disease and elsewhere.

Population Statistics

From measurements on the individual and on defined morbid groups, we turn, thirdly, to measurements on populations – vital or population statistics, though there is no sharply defined line of demarcation between the three categories.

The acknowledged father of vital statistics is John Graunt, who in 1662 published his 'Natural and Political Observations upon Bills of Mortality'. The London Bills had been kept for about a hundred years, and regularly for seventy years, before John Graunt examined them. He showed, for example, that more boys are born than girls although the excessive mortality in male infants soon reversed the trend; that the rural life was more healthy than the urban; and that a population can be estimated from an accurate death rate.

Twenty-five years later, Sir William Petty, who had taken the first census in Ireland, published his 'Essays on Political Arithmetic', and in 1693, the English astronomer, Edmund Halley, compiled the 'Breslau Table of Births and Funerals' in order to reveal the proportion of men able to bear arms in any community, to estimate its mortality rates, to ascertain the price of annuities upon lives, and so forth.

By 1829, F Bisset Hawkins (who finds no place in Garrison's 'History of Medicine') had published his Goulstonian Lectures on 'Elements of Vital Statistics'. In 1842, Edwin Chadwick had initiated the sanitary era of public hygiene by emphasizing the lessons to be drawn from a study of the census and Bills of Mortality. William Farr was furthering the cause of statistics in sickness by contributing to McCulloch's 'Statistical Account of the British Empire', published in 1837, which led to his fruitful appointment to the General Register Office. His contemporary, John Snow, was in 1849 to make the handle of the Broad Street pump immortal, despite historical doubts since expressed, by his use of the statistical method to demonstrate that cholera is waterborne and taken into the system by mouth.

Unfortunately, the dramatic triumphs of bacteriology in demonstrating the specific and necessary causes of certain diseases overshadowed for a time the importance of studying environmental factors by statistical methods.

The knowledge that physical characteristics are inherited stems from ancient times, but it was the simple measurements of Gregor Mendel in 1866, rediscovered in 1900, which were to lay firmly the foundations of modern genetics and its application to disease. There are few fields which reveal so strikingly the fruitful synthesis of biologist, mathematician, physicist, chemist, radiologist and others.

Towards the end of the nineteenth century came the brilliant school of biometricians led by Galton, Karl Pearson, and later R A Fisher and Bradford Hill, who were to introduce probability statistical methods in the analysis of the causation of disease, and in the design and interpretation of clinical trials of therapeutic substances.

With the rapidly accelerating growth of scientific and technical knowledge in this century, and with the inevitable trends towards specialization, those working in one discipline tend to move further and further away from those working in another as the methods of investigation become more complex, and for each other more forbidding. This Section will, it is hoped, break down barriers. The specialties diverging from their mother-stem will converge in this Section. Here we will seek to find how techniques so valuable and fruitful in other fields can be harnessed to the needs of medicine and surgery. Here investigators who have developed techniques in one branch of medical science will make others aware of them. Too often these are buried in the archives of specialties and their wider application fails to be appreciated. Here also will be a forum where workers of like interests and purpose can meet and discuss their mutual problems, and who knows but that the chance comment or suggestion emerging in discussion or social intercourse, may stimulate the uncovering of a hitherto hidden truth. Here colleagues in many fields – physicists, chemists, mathematicians, engineers and others – can meet us and help us with their specialized knowledge and skills to devise measuring instruments and techniques more rapid, more accurate, and more appropriate to our special needs, and help us also to analyse and interpret our data by the use of modern statistical tools and computer analysis.

In short, there lies behind the concept of this Section a desire for a synergy and symbiosis of doctors, scientists and technologists, for their mutual advantage. It is a concept of exciting potentiality. Helmholtz, following Galileo, declared that 'all science is measurement'. No clinician is likely to concede this aphorism without reservations. But though measurement in medicine may not be an end in itself it is, as history reveals, of fundamental importance to the advancement of medical science. It is because the Royal Society of Medicine holds that the work of this Section, alone and in joint discussions with other Sections, has an invaluable contribution to make to medicine, that on behalf of the Society I tender the Section congratulations on its birthday and wish it many happy returns.